IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Gleave, et al. Application No.: 09/913,325 Filed: 8/10/2001 Title: TRPM-2 Antisense Therapy Attorney Docket No.: UBC.P-020 Customer No.: 57381	Group Art Unit: 1635 Examiner: Tracy Vivlemore Confirmation No: 8469

Commissioner for Patents

PO Box 1450

Alexandria, VA 22313-1450

RESPONSE TO FINAL REJECTION

Dear Sir:

This is in response to the Office Action mailed November 14, 2006 for the above-captioned application. Reconsideration and further examination are respectfully requested.

Applicants that the Examiner for taking the time to meet with their attorney. This paper will serve as a summary of that interview.

Claims 6, 8, 10, 12-17, 31 and 32 stand rejected under 35 USC § 103 as obvious over the Bruchovsky, in view of Sensibar, Kyprianou and Raghavan. As discussed at the interview, Applicants believe that there are several legal and factual errors in the explanation of the rejection, and that the claims are properly allowed.

First, the Examiner characterizes Sensibar as teaching TRPM-2 gene therapy. Applicants respectfully submit that the Sensibar paper does not deal with gene therapy. Indeed, in the Sensibar paper, the LNCaP cells are first transfected to introduce a vector that will lead to TRPM-2 (SGP-2, clusterin) expression so that the effect of suppressing this expression can be observed. There is no teaching or suggestion in the paper of a therapeutic use of reducing TRPM-2 expression.

Second, as pointed out in the interview, while Sensibar teaches that increased TRPM-2 **could** protect from TNF alpha toxicity, there is no connection in the cited art between TNF-alpha and androgen withdrawal as described in the Bruchovsky paper.

Thirdly, during the interview, the standard for a reasonable expectation of success was discussed. It is important to recognize that the standard for a reasonable expectation of success must be something more than "it might work." In the present case, Dr. Gleave has explained through his declaration that the statement in the Bruchovsky paper on which the Examiner relies is merely an indication of the direction of future experiments, and that the state of the art at the time was such that the outcome of these experiments could not have been predicted. As such, this statement is nothing more than an invitation to experiment, which is not a valid basis for a finding of obviousness.

In the official action (page 3), the statement is made that:

> The examiner acknowledges that the effect of a decrease in TRPM-2 on apoptosis might not have been known, but this is not required by the claims, which recites that the TRPM-2 antisense inhibits expression of TRPM-2.

This argument is not understood. If the effect of a decrease in TRPM-2 on apoptosis was not known, then it was not known and could not be predicted that a decrease in TRPM-2 would lead to any therapeutic benefit. Thus, there was no reasonable expectation of success.

The Examiner also states that Dr. Gleave's statement that the outcome of the experiments proposed in Bruchovsky was unpredictable is contradicted by Bruchovsky's statement that "this was a viable direction for future research." (Office Action, Page 4) This argument assumes that no one would ever suggest performing an experiment unless they were reasonably sure of the outcome, which seems contrary to the history of science.

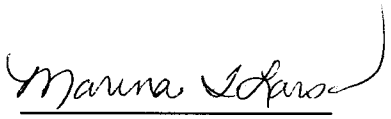
The Examiner also stated that the evidence relating to the synergistic effect of TRPM-2 and chemotherapy agents is not commensurate in scope with the claims, because there was no androgen withdrawal step included in the experiment. As explained at the interview, however, androgen withdrawal is relevant in an *in vivo* context where there are sources for androgen to be suppressed. In a cell culture model as used in the experiments, however, androgen is absent unless it is added, and therefore androgen withdrawal as a separate step is not needed.

Finally, Applicants pointed out that the Examiner's reliance on Raghavan was essentially an argument that once some combination of chemotherapy agents was known, all other combinations are obvious. Applicants submit that this is inconsistent with the law, which

requires a suggestion of the claimed invention, not an invitation to experiment within some broad genus to which the claimed invention belongs.

In view of the foregoing, Applicants submit that all of the claims of this application are in form for allowance, and such action is earnestly solicited.

Respectfully submitted,



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